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14. ABSTRACT
Nearly one million Americans suffer from chronic fatigue syndrome (CFS). More than 15% of Gulf War veterans (GWV) were found to have CFS. The disease significantly reduces work production of civilian patients and combat ability/readiness of US military forces. Increasing scientific evidence suggests that CFS is a biological illness involving pathology of the central nervous system (CNS). However, little is known about how the CNS is affected by CFS. This study will focus on evaluating brain activities of CFS patients during fatigue and non-fatigue muscle exercises. Our hypothesis is that the brain activation pattern in CFS differs from that of healthy controls. Aim 1 of the study is to determine brain activation patterns during motor activity in CFS patients using functional magnetic resonance imaging. Aim 2 is to examine brain activation patterns during motor activity in CFS patients by analyzing signals of electroencephalograms. Aim 3 is to evaluate signal relationships among different brain regions and between the brain and muscle. Measurements will be made from four groups of participants: a civilian CFS group, a civilian control group, a GWV CFS group, and a GWV control group. We expect that the study will provide objective information for diagnosis of CFS.

15. SUBJECT TERMS
Chronic fatigue syndrome, Gulf War Syndrome, functional MRI, electroencephalogram (EEG) 15. Number of Pages (count all pages including appendices) Electromyogram (EMG), brain motor activity, brain activation pattern, EEG frequency

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Table of Contents

Introduction

Chronic fatigue syndrome (CFS) is an illness that affects quality of life of both civilian and military populations. However, the diagnosis of CFS is difficult to make because of the absence of specific biomedical markers. Thus, the diagnosis depends primarily on determining whether subjective information provided by the patient meets the clinical case definition of the syndrome. The purpose of this study is to determine whether the central nervous system signals of CFS patients for performing fatigue and non-fatigue motor activities are impaired compared to the signals of healthy volunteers. It is hypothesized that the CNS signals of CFS patients will significantly differ from those of healthy controls. It is expected that at least one or more measurements made by this study will serve as "biological markers" for more objective diagnoses of CFS.

BODY

This report covers the third year of work related to this study. So far, a manuscript based on the results of the analyzed data has been published in the journal of *Clinical Neurophysiology*. A second paper supported by this grant is in press in the journal of *Brain Research*. In addition, A number of studies that were jointly supported by this grant and other awards (mainly from NIH) have been accepted for publication or are already in press. Further analyses of data collected in the past three years are ongoing and more publications are expected in the future. Work that performed in the last year of the project included:

I. *Recruiting and testing research subjects*. We have collected data from a total of 58 human subjects. The manuscripts that have published and those to be published soon are based on data collected from these subjects.

II. *Developing data analysis software and performing data analysis.* We have developed two software packages for the analysis of electroencephalogram (EEG) and electromyogram (EMG) data. We used these software packages to analysis the collected data and have reported a large portion of the results in the published and in-press manuscripts. Further and more sophisticated data analysis is underway and we anticipate that the new results will lead additional publications. New data analysis include mapping of the electrical signals recorded from the scalp during motor performance using high-density EEG recordings and characterizing differences in frequency modulation and functional connectivity between the brain and muscle in patients and control subjects when they performed motor tasks that induced fatigue.

KEY RESEARCH ACCOMPLISHMENTS

I. A number of manuscripts have been published or will be published soon in high-quality clinical and scientific journals (see References).

II. Eight presentations on the topic of this study have been made at regional, national, and international scientific conferences

REPORTABLE OUTCOMES

I. Motor performance of the CFS patients was poorer than the controls.

II. Relative power of EEG theta frequency band (4-8 Hz) during performing a non-fatigue (NFT) and fatigue (FT) task was significantly greater in the CFS than control group ($P < 0.05$).

III. The amplitude of negative potential (NP), a major component of EEG-derived movement-related cortical potential for the combined NFT and FT tasks was higher in the CFS than control group ($P < 0.05$).

IV. Within the CFS group, the NP was greater for the FT than NFT task ($P < 0.01$), whereas no such difference between the two tasks was found in the control group.

V. Compared to healthy individuals, the EEG source of the CFS patients shifted towards anterior-inferior location of the brain during the fatigue task.

VI. The source strength was different between the CFS and control groups during both the fatigue and non-fatigue tasks.

VII. Developed methods to quantify physiological connection (signal coherence) between the brain and muscle.

VIII. Developed methods to quantify brain white matter structures.

CONCLUSIONS

The results show that chronic fatigue syndrome involves altered central nervous system signals in controlling voluntary muscle activities, especially when the activities induce fatigue. Physical activity-induced EEG signal changes may serve as biological/physiological markers for more objective diagnosis of CFS.

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